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10/581,545	11/14/2008	**Giles Albert Brown**	13425-192US1 BV-1087 US	3942

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FISH & RICHARDSON PC
P.O. BOX 1022
MINNEAPOLIS, MN 55440-1022

EXAMINER	
CRANE, LAWRENCE E	
ART UNIT	**PAPER NUMBER**
1623	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PATDOCTC@fr.com

Office Action Summary	Application No.	Applicant(s)	
	10/581,545	BROWN ET AL.	
	Examiner	Art Unit	
	Lawrence E. Crane	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *October 29, 2009 (amendment)*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14,18-35,37,38 and 40-44* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *14* is/are allowed.

6)☒ Claim(s) *1-14,18-35,37,38 and 41-44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

The Abstract of the Disclosure is objected to because is does not meet the requirement of the MPEP for US application. Correction is required. See MPEP §608.01(b).

Applicant is reminded of the proper content of an Abstract of the Disclosure.

In chemical patent abstracts, compounds or compositions, the general nature of the compound or composition should be given as well as its use, e.g., "The compounds are of the class of alkyl benzene sulfonyl ureas, useful as oral anti-diabetics." Exemplification of a species could be illustrative of members of the class. For processes, the type reaction, reagents and process conditions should be stated, generally illustrated by a single example unless variations are necessary. Complete revision of the content of the abstract is required on a separate sheet.

Applicant is respectfully requested to amend the Abstract because the Abstract is not in US format and is also excessively brief.

Applicant's arguments filed October 29, 2009 have been fully considered but they are not persuasive.

Examiner notes applicant's submission of an amended Abstract. Said Abstract cites the Disclosure as a source of definitional information that should be, and was previously, part of the Abstract. Variable R should be defined in the Abstract. Appropriate re-correction is respectfully requested.

Claim **39** was previously cancelled, claims **15-17 and 36** have been newly cancelled, claims **3, 7-10, 13, 18-23, 25, 27-31, 38, and 41-44** have been amended, the disclosure has been amended, the Abstract has been amended, and no new claims have been added as per the amendment filed October 29, 2006. No additional or supplemental Information Disclosure Statements (IDSs) have been filed as of the date of this Office action.

Claims **1-14, 18-35, 37, 38 and 40-44** remain in the case.

Note to applicant: when a rejection refers to a claim **X** at line y, the line number "y" is determined from the claim as previously submitted by applicant in the most recent response including ~~lines deleted by line through~~.

Claims **1, 20, 21, 27 and 29** are objected to because of the following informalities:

In claim **1** at lines 5, 7 and 8, the term "CF_3-" is technically erroneous or includes a typographical error. Did applicant intend the term to read -- -CF_3 --? See also claims **20, 27 and 29** wherein the same error reoccurs.

Appropriate correction is required.

Claims **1-14, 18-35, 37, 38 and 41-42** are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Factors to consider in this analysis:

a) Actual Reduction to Practice? Examiner has carefully reviewed the prior art cited (Deghati et al. and the Wanner et al. reference (PTO-1449 ref. **AM**; cited in applicant's disclosure at pages 2 and 3)) in addition to applicant experimental disclosures plus the contents of Schemes 1 and 2, and notes that both Schemes are now included in amended claim **38**. While the contents of Schemes 1 and 2 are reproduced at the end of the disclosure (see pages 20-21), the process details therein for the synthesis of "adenosine pentaacetate" differs noticeably when compared to the process disclosed at page 18 (Example 5), ands both disclosed processes differ noticeably from the contents of many claims wherein a process or processes for the synthesis of "adenosine pentaacetate" are claimed (e.g. see claim **25** and the newly added term "further acetylated," a process step not described in any disclosed exemplification including in the Schemes). Examiner also notes that the written and schematic descriptions of the processes for making 2-nitroperacylated adenosines do include the presence of both a nitrate salt and trifluoroacetic anhydride, but that the instant claims (see claim **7** for example) only note the presence of the nitrate salt " ... as a nitrating agent." Examiner wonders how applicant has caused a nitrate salt to act as a nitrating agent in the absence of trifluoroacetic anhydride (TTFA), when both the Deghati and Wanner references require TTFA as an essential part of the nitration process, apparently in order to react with nitrate ion to generate a mixed nitric/trifluoroacetic anhydride (CF_3-(C=O)-O-NO_2) that ionizes to generate the nitronium ion (NO_2^+) intermediate that reacts at the C-2 of either of the instant penta-acylated adenosine coreactants.

Examiner also notes that there are appear to be no specific embodiments providng a written description of the "trituration" with isopropanol and the "washing" with water steps specified in several claims (e.g. claims **8, 20 and 42**), another situation wherein there is doubt concerning whether applicant actually had possession of the entirety of the claimed subject matter as of the filing date.

b) Disclosure of Drawings, Structural, and Other Chemical Formulas? The glaring inconsistencies between the process details in the Schemes 1 and 2, the written description of the same processes, and the claimed processes are noted in the previous paragraph.

c) Sufficient relevant identifying characteristics? This factor is not applicable in the instant analysis.

d) Method of making the claimed invention? This factor is dealt with in the first paragraph of this analysis above.

e) Level of skill in the art? This factor is not applicable in the instant analysis.

f) Predictability in the art? The nitration of peracylated adenosines is known in the art, but the reagent used is not completely described as part of the instant claimed nitration process steps, and there is no written description of a process wherein trifluoroacetic anhydride (TTFA) is not present to active nitrate ion. Therefore, the claims wherein nitration of peracylated adenosine is claimed in the absence of TTFA are found to lack predictability based on what is known in the prior art about this process and what has been added to the prior art by the disclosed specific embodiments.

The instant claims are found to lack a clear and unequivocal basis in the written description including Schemes 1 and 2 because there is no disclosure therein of how to induce a nitrate ion alone, introduced as part of a quaternary ammonium nitrate salt, to participate in the nitration of any organic molecule to make a nitro compound, including the nitration of a peracylated adenosine at the C-2 position.

Applicant's arguments with respect to claims **1-38 and 40-44** have been considered but are moot in view of the new grounds of rejection. This new ground of rejection was necessitated in part by applicant's amendments.

Claims **1, 3, 5, 6, 8, 10-12, 19, 20, 22, 25-30, 32-34, 41 and 43-44** are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim **1** at line 2, the term "converting" standing alone is insufficient to adequately describe the process step or steps required to execute the claimed process wherein 2-nitro-pentabenzoyladenosine is converted into the variety of 2-substituted adenosines encompassed by the subject matter disclosed at lines 3-8. See also claims **3** ("converted ... by deprotection"), **5, 6, 11, 12 and 22**("produced ... by deprotecting") wherein the same or similar errors reoccur.

Applicant's arguments filed October 29, 2009 have been fully considered but they are not persuasive.

Applicant argues that the term "converting" and other generic terms unaccompanied by the specifics of a chemical process step are sufficient and consequently that the above rejection should be withdrawn because there is no reason given for the rejection of said terms. Examiner respectfully disagrees and finds that applicant has failed to understand that the term "converting," for example, may be applied to many processes that are not chemical, including -- converting waste paper into pulp --, -- converting DC electricity to AC electricity --, -- converting an analog signal into a digital signal --, etc.

In order to establish the properly defined metes and bonds of a process step as a chemical process step, applicant is respectfully requested to add the minimum necessary reagents and/or reaction conditions necessary to carry out the claimed "converting" step, and to the other process steps now also missing the minimum reagent/reaction condition information necessary to understand the metes and bounds of the particular chemical process step being defined. Otherwise the generic term "converting" standing alone is meaningless, and the claims are in effect nothing more than lists of compounds, a reality that is in direct conflict with the preamble term "method of synthesizing" found at line 1 of claim **1** for example.

At pages 20-21 of applicant's response, in the sentence bridging said pages, applicant alleges that " ... claim [**1**] describes a specific synthetic route for preparing the defined 2-substituted adenosine." Applicant's analysis is factually incorrect because claim **1** has failed to provide a chemical reagent or reagents necessary to achieve the asserted "converting" process, an element the absence of which reduces claim **1** to nothing more than a description of a

starting material (2-nitropentabenzoyladenosine) and a generic class of products which are 2-alkoxysubstituted adenosines. As a practitioner familiar with nucleoside chemistry, examiner had no difficulty in "guessing" the likely process being claimed, i.e. alkoxide displacement of the 2-nitro substituent of the starting material and subsequent alkoxide reaction with the benzoyl protecting groups (deprotection) to generate in a single reaction pot the desired product, a 2-alkoxyadenosine. The presence of excess alkoxide ion is required to insure that both the 2-nitro displacement step and the deprotection steps occur and go to completion, thereby minimizing the need for subsequent separation of product mixtures.

But, at present the patent claim does not say this, and therefore cannot be defended as providing protection for the "converting" process as presently claimed because the process has not been completely defined.

Examiner respectfully suggests that inserting into claim **1** at the beginning of line 5 the term -- by contacting the starting material with a greater than a six Molar excess of $R\text{-}O^{-}\ M^{+}$ (an alkoxide metal salt wherein M^{+} is Li^{+}, Na^{+} or K^{+}) in a suitable solvent -- as one way to address this problem. Examiner does not guarantee that no other problems would be caused by this change and suggests careful consideration of the possible need for additional amendments to avoid lack of antecedent basis issues.

Appropriate amendment of the claim **1** and other claims wherein the noted "missing reagent information" problem occurs, and sometimes reoccurs, is respectfully requested. See in particular claims **5-7, 11, 12, 20, 24-30, 32-34, 41 and 43-44**.

In claim **3** at line 4, the term "deprotecting protected functional groups" renders the noted claim lacking in proper antecedent basis because a deprotection step is not included in claim **1**. In light of the well known in the art capability of alkoxide anions to induce deacetylation or debenzoylation of acyl derivatives of nucleosides, examiner presumes that this problem is readily solved by simply noting in an amended claim **1** that both 2-nitro displacement and acyl group removal are achieved concomitantly by a greater than 6 Molar excess alkoxide anion in a single reaction vessel, at least in some cases. In addition to the Deghati and Wanner references, see the Kochetkov et al. references now made of record (PTO-892 ref. **U and V**) wherein problems with some nucleoside deacylation reactions are disclosed.

Applicant's arguments with respect to claims **1-38 and 40-44** have been considered but are moot in view of the new grounds of rejection. This new ground of rejection was necessitated by applicant's amendments.

In claim **8** the term "reducing the amount of TBAN or TMAN" is incomplete because the process step or steps being claimed have not been adequately described. See also claim **20** at lines 3-4 wherein the same error reoccurs.

Applicant's arguments filed October 29, 2009 have been fully considered but they are not persuasive.

After quoting the functional claim language in question, applicant argues that one of ordinary skill would know that the term "reducing" in claim **8** is intended to refer to a -- washing step -- wherein the excess quantity of a coreactant is -- reduced -- by said washing. Examiner respectfully disagrees and does not think that it should be necessary for the claim to have to be interpreted by reading the specification when by simply describing the entire step in the claim would suffice; e.g. -- which further comprises <u>washing with water to reduce</u> the amount of [TBAN] ...-- or the like. Appropriate amendments generating complete descriptions of this process step within both claims **8 and 20** are respectfully requested.

In claim **10** the term "recrystallizing" (the US spelling differs from the British spelling of this term) is a process step but has not been completely described because the presence of a solvent or solvents have not been included in the claim. See also claim **19** wherein the same error reoccurs.

Applicant's arguments filed October 29, 2009 have been fully considered but they are not persuasive.

Applicant argues that recrystallization is so well understood that one of ordinary skill would be expected to be 100% accurate in a guess that a solvent would be used and also 100% accurate in the kind of solvent and/or solvent mixture that is being hinted at by the generic term "recrystallization." Examiner respectfully disagrees and does not consider hints in the form of generic terms standing alone to be sufficient as a basis for determining the metes and bounds of claimed subject matter. Applicant is respectfully requested to specify the solvent and/or solvent mixtures intended to be claimed in the noted claims. Correction of the term

"recrystallisation" (all occurrences) to US spelling (-- recrystallization --) is also respectfully requested in claims **10 and 19**.

In claim **22** at lines 1-3, it is unclear whether the "deprotecting" and the "reaction with ... alkoxide anion or phenoxide anion" are both happening simultaneously courtesy of the named reagents. Either a clarifying explanation or an amendment is respectfully requested.

Applicant's arguments filed October 29, 2009 have been fully considered but they are not persuasive.

Applicant asserts that both nitro group displacement and acetyl group removal occur simultaneously and that the "plain language of the claim" makes this clear. Examiner agrees with the chemistry asserted, but notes that the admission supports examiner's view that claim **22** now lacks proper antecedent basis in claim **20** wherein no mention is made of deprotection. Applicant is referred to comments made above concerning a similar problem concerning claims **1 and 3** wherein amendment of claim **1**, and herein claims **20 and 22**, seems appropriate as one possible solution to the antecedent basis problem. An appropriate clarifying amendment of one or both claims is/are respectfully requested.

In claim **23** at line 2-3, the term "process comprising deprotecting the 2-nitroadenosine" is lacking in proper antecedent basis (claim **20** does not mention "deprotecting") and neither claim **20** nor claim **23** mentions the probable need for the -- excess alkoxide -- needed to insure complete displacement and deprotection reactions. Also neither claim teaches that both displacement and deprotection occur simultaneously in the same reaction vessel. Amendments adequately correcting the noted deficiencies including the lack of proper antecedent basis are respectfully requested.

Applicant's arguments with respect to claims **1-38 and 40-44** have been considered but are moot in view of the new grounds of rejection. This new ground of rejection was necessitated in part by applicant's amendments.

In claim **24** at line 2, the term "acylating" is inconsistent with the named product, "adenosine pentaacetate." Examiner respectfully suggests that the noted term may be amended to read -- peracetylated -- as one possible replacement for the noted term. In addition, claim **24** does not specify any reagent(s) and therefore needs to be amended to include possibly

-- acetic anhydride --, and further -- 4-dimethylaminopyridine (DMAP) -- as provided for in process step 1 of Schemes 1 and 2. Appropriate amendments are respectfully requested.

Applicant's arguments with respect to claims **1-38 and 40-44** have been considered but are moot in view of the new grounds of rejection.

In claim **25** the term "acylated" appears twice but, because the products of the two process steps claimed are different, the process conditions must be different. Clarification of the obviously differing meanings of the term "acylating" is respectfully requested. See also claims **27, 29 and 43** wherein the same problem reoccurs.

Applicant's arguments filed October 29, 2009 have been fully considered but they are not persuasive.

As noted in the new ground of rejection supra made under 35 U.S.C. §112, first paragraph, there is no disclosed method of synthesis wherein the above claimed subject matter has been described and further examiner notes that Schemes 1 and 2 do not provide for a second "acylation" step. Applicant argues based on the face of the claim that two steps are recited, but fails to note that there is no written description to fill in the details of how this "two step process to produce a peracetylation of adenosine" is actually carried out. No disclosure has been provided in any specific embodiment or in either of Schemes 1 and 2 of the details presented in claims **25, 27, 29 and 43**. A clarifying explanation or other appropriate action is respectfully requested.

In claim **26** the term "washing" is generic" with no particular details of the actual process step having been specified, and therefore the claimed process step is incompletely described. See also claims **28, 29 and 44** wherein the same error reoccurs.

Applicant's arguments filed October 29, 2009 have been fully considered but they are not persuasive.

The generic term "washing is found by applicant to be clear and definite. Examiner respectfully disagrees because the particular solvent that is doing the "washing" has not been specified, leaving one of ordinary skill to consider all possible washing solvents, an example of guess work. In addition, as noted above, there is no specific embodiment disclosed herein that

specifies the details of how said washing is to be carried out, only the occasional mention in the occasional other claim that "water" is the wash solvent. If applicant is serious about obtaining patent protection for this claimed subject matter, examiner respectfully suggests that submission of additional data (in a declaration under 37 C.F.R. §1.132) to add the missing description of the "washing step(s)" is one route to solving the problem. Appropriate amendment or other action is respectfully requested.

In claims **27 and 29** the term "formula 1" is now completely defined because a chemical formula has been added to the claim. However, in the last 4 lines of this claim, the term "acylating" is technically erroneous (the process can be only -- acetylating --), there is no specific embodiment describing the separation of adenosine tetraacetate from adenosine pentaacetate, and the process step implied by the term "producing" in last two lines is missing the necessary reagent(s) to effect the conversion of 2-nitroadenosine pentaacetate into a 2-alkoxy adenosine. Therefore, while claims **27 and 29** are now more complete, the claimed process steps hinted at therein by the terms "acylating" and "producing" have not been adequately defined by including the identification of the reagents necessary to carry out the process steps, and all of the process steps have not been listed: e.g. -- deprotection -- is not mentioned even though it occurs concomitantly with nitro group displacement. Appropriate amendment or other action is respectfully requested.

Applicant's arguments with respect to claims **1-38 and 40-44** have been considered but are moot in view of the new grounds of rejection. This new ground of rejection was necessitated in part by applicant's amendments.

In claim **29** at the last two lines, the term "producing the 2-substituted adenosine from the washed adenosine pentaacetate" summarizes several chemical process steps, wherein the number of process steps varies depending on whether or not the 2-nitroadenosine intermediate is subject to chloride ion displacement prior to reaction with an alkoxide reagent (see Schemes 1 and 2). Applicant is respectfully requested to specify by appropriate amendment each and every process step implied by the term "to produce" in order to make the noted claim complete, or to take other appropriate action.

Applicant's arguments with respect to claims **1-38 and 40-44** have been considered but are moot in view of the new grounds of rejection.

In claim **30** the term "nitrating" is incomplete because -- the reagent(s) -- required to effect this process step(s) has(have) not been disclosed in the claim, thereby rendering the claim incomplete.

Applicant's arguments filed October 29, 2009 have been fully considered but they are not persuasive.

Applicant argues that the noted claim is directed to " ... a process in which a 'nitrating step' is performed - not one where nitration is performed with particular reagents." Examiner agrees with this characterization and notes that this breadth of claim language is not supported by the instant disclosure as noted above in the first rejection now of record. Applicant is encouraged to introduce the specific reagent (nitrate ion plus trifluoroacetic anhydride) that is known in the prior art to permit adenosine pentaacetate to be 2-nitrated, and that is described herein as a reagent combination effective to achieve that same result with two different penta-acylated adenosine starting materials. Applicant is respectfully requested to amend the instant claim or to take other appropriate action.

In claim **32** the process step whereby 2-nitroadenosine is "converted" into 2-chloroadenosine is claimed, but has not been described, thereby rendering the instant claimed process incompletely described in this claim. Said claim is also incomplete because the subsequent term "producing" implies a chemical process step but fails to identify the reagent(s) necessary to effect said step or steps (nitro group displacement by chloride ion following by chloride ion displacement by alkoxide). See also claims **33 and 34** wherein the same or a very similar errors of incompleteness reoccur.

Applicant's arguments with respect to claims **1-38 and 40-44** have been considered but are moot in view of the new grounds of rejection.

In claim **35** at line 3, the term "by reaction with methoxide anion:" is incomplete and may be amended to read -- by reaction of excess methoxide anion --. The proposed change corrects a grammatical error and adds a limitation that is necessary to permit the claimed subject matter to correspond to the process steps that actually occur (nitro group displacement and complete acetyl protecting group removal) only when excess methoxide is present.

Applicant's arguments with respect to claims **1-38 and 40-44** have been considered but are moot in view of the new grounds of rejection.

In claim **38** in both Scheme 1 and Scheme 2, there are numerous acronyms (e.g. "DMAP" (aka 4-dimethylaminopyridine??) that have not been defined, thereby rendering this claim incomplete. Applicant is respectfully requested to supply by amendment the definitions of each and every acronym by amendment. In addition, in this claim at line 2, the term "scheme" should be capitalized in order to properly refer to the titles beneath the subsequently provided "Scheme[s]."

Applicant's arguments with respect to claims **1-38 and 40-44** have been considered but are moot in view of the new grounds of rejection. This new ground of rejection was necessitated by applicant's amendments.

In claim **41** at lines 3-4, the term "reducing" implies a process step that has not been described with sufficient detail, thereby rendering this process step incompletely described in this claim. See also claim **44** wherein the same error reoccurs.

Applicant's arguments filed October 29, 2009 have been fully considered but they are not persuasive.

Applicant is referred to the comments followng the rejection of claims **8 and 20** supra wherein the same or a very similar incompletely defined term generically referring to a process step is discussed.

In claim **43** at lines 1-2 refers to two different -- acetylating --processes, but has failed to describe what reagent or reagents are necessary to carry out the claimed process wherein adenosine pentaacetate is the final product. Earlier claims suggest that "washing" step or steps may be necessary, but the disclosure fails to include even a single example wherein applicant has disclosed the details of said washing steps. A clarifying amendment and/or explanation and or additional experimental disclosure (1.132 declaration?) is/are respectfully requested. See also claim **44** wherein the same error reoccurs.

Applicant's arguments with respect to claims **1-38 and 40-44** have been considered but are moot in view of the new grounds of rejection. This new ground of rejection was necessitated by applicant's amendments.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. §102 that form the basis for the rejections under this section made in this Office action:

"A person shall be entitled to a patent unless -

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent."

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States."

(e) the invention was described in

(1) an application for patent described under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application filed under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or

(2) a patent granted on an application by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a)."

(f) he did not himself invent the subject matter sought to be patented."

Claims **20-35, 37, 38 and 40-44** are rejected under 35 U.S.C. §102(**b**) as being anticipated by **Wanner et al.** (PTO-1449 ref. **AM**).

Applicant is referred to **Wanner et al.** at pages 2141-2142 including "Scheme 1" wherein this reference discloses the conversion of adenosine into 2-methoxyadenosine via a three step process that appears to anticipate the instant claimed processes, including the synthesis of adenosine pentaacetate by peracetylation of adenosine, the conversion of adenosine pentaacetate into 2-nitroadenosine pentaacetate by contact with a quaternary ammonium nitrate/trifluoroacetic anhydride mixture, and the conversion of 2-nitroadenosine pentaacetate by contact with methoxide ion into 2-methoxyadenosine. Therefore, the instant cited **Wanner** reference anticipates both the chemical processes starting with the peracetylation of adenosine and the product named in claim **40**.

Applicant's arguments with respect to claims **1-38 and 40-44** have been considered but are moot in view of the new grounds of rejection. This new ground of rejection was necessitated by applicant's amendments.

Claim **40** is rejected under 35 U.S.C. §102(**b**) as being anticipated by **Ueeda et al. (I)** (PTO-892 ref. **S**).

Applicant is referred to Table 1 at page 1335 and associated explanatory text at pages 1334-1335 wherein the details of the synthesis, the process of isolation (following deprotection) , and the physical characteristics of the pure compound "3a" (2-methoxyadenosine, aka spongosine) are disclosed. Therefore the instant claimed subject matter has been anticipated.

Applicant's arguments with respect to claims **1-38 and 40-44** have been considered but are moot in view of the new grounds of rejection. This new ground of rejection was necessitated by applicant's amendments.

The following is a quotation of 35 U.S.C. §103(**a**) which forms the basis for all obviousness rejections set forth in this Office action:

> "A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made."

Claims **20-35, 37, 38 and 40-44** are rejected under 35 U.S.C. §103(**a**) as being unpatentable over **Wanner et al.** (PTO-1449 ref. **AM**).

The instant claims are directed to the conversion of adenosine into 2-methoxyadenosine via a three step process that appears to anticipate the instant claimed processes, including the synthesis of adenosine pentaacetate by peracetylation of adenosine, the conversion of adenosine pentaacetate into 2-nitroadenosine pentaacetate by contact with a quaternary ammonium nitrate/trifluoroacetic anhydride mixture or with the quaternary ammonium nitrate alone, and the conversion of 2-nitroadenosine pentaacetate by contact with methoxide ion into 2-methoxyadenosine.

Wanner et al. discloses at pages 2141-2142 including "Scheme 1" the conversion of adenosine into 2-methoxyadenosine via a three step process that appears to anticipate the instant claimed processes, including the synthesis of adenosine pentaacetate by peracetylation of adenosine, the conversion of adenosine pentaacetate into 2-nitroadenosine pentaacetate by contact with a quaternary ammonium nitrate/trifluoroacetic anhydride mixture, and the conversion of 2-nitroadenosine pentaacetate by contact with methoxide ion into 2-methoxyadenosine.

Wanner et al. does not expressly disclose multiple acetylation steps without 4-dimethylaminpyridine present as a catalyst in the process of generating adenosine pentaacetate from adenosine or any washing steps to separate adenosine pentaacetate from adenosine tetraacetate or other di- and tri-acetates of adenosine. This reference also does not disclose that nitration is possible in the presence of quaternary ammonium nitrate salts and in the absence of trifluoroacetic anhydride, and does not disclose any washing steps following the nitration step wherein residues of quaternary ammonium salts are removed from the 2-nitroadenosine pentaacetate product.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to attempt by routine experimentation the optimization of the prior art **Wanner et al.** process. The optimization would be expected to include improving yields by improving the purity of intermediate and final products by applying standard organic chemical methodologies including washing and/or recrystallization to improve the purity of process intermediates, or apply other routine experimentations to the variation of other operating variables in the process steps disclosed by the **Wanner et al.** reference.

One having ordinary skill in the art would not have needed to be motivated because routine optimization is a well known in the art process for the exploration of the metes and bounds of the prior art.

Therefore, the instant claimed method of synthesizing 2-methoxyadeosine via nitration of adenosine pentaacetate, and the compound 2-methoxyadenosine, would have been obvious to one of ordinary skill in the art having the above cited reference before him at the time the invention was made.

Applicant's arguments with respect to claims **1-38 and 40-44** have been considered but are moot in view of the new grounds of rejection. This new ground of rejection was necessitated by applicant's amendments.

Claim **14** appears to be allowable as submitted.

Claims **1-13, 18 and 19** would be allowable if rewritten or amended to overcome the rejections under 35 U.S.C. §112 set forth in this Office action.

This Office action includes several new grounds of rejection and therefore is a non-final rejection.

Papers related to this application may be submitted to Group 1600 via facsimile transmission (FAX). The transmission of such papers must conform with the notice published in the Official Gazette (1096 OG 30, November 15, 1989). The telephone number to FAX (unofficially) directly to Examiner's computer is 571-273-0651. The telephone number for sending an Official FAX to the PTO is 571-273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner L. E. Crane whose telephone number is **571-272-0651**. The examiner can normally be reached between 9:30 AM and 5:00 PM, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ms. S. Anna Jiang, can be reached at **571-272-0627**.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose telephone number is **571-272-1600**.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status Information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see < http://pair-direct.uspto.gov >. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at **866-217-9197** (toll-free).

LECrane:lec
02/19/2010

/Lawrence E. Crane/

Primary Examiner, Art Unit 1623

L. E. Crane
Primary Patent Examiner
Technology Center 1600